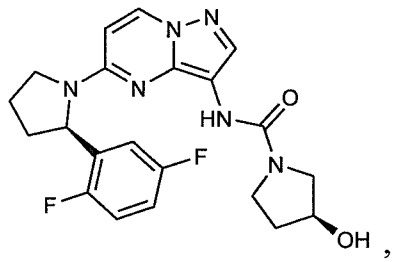
WO 2010/048314 discloses in Example 14A a hydrogen sulfate salt of (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide. WO 2010/048314 does not disclose the particular form of the hydrogen sulfate salt described herein when prepared according to the method of Example 14A in that document. In particular, WO 2010/048314 does not disclose crystalline form (I-HS) as described below.

All documents, including scientific articles, patent publications and applications, and the like, referenced in the present disclosure are hereby incorporated by reference in their entirety.

SUMMARY

In one aspect, there is provided a liquid formulation comprising a solubilizing agent and (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

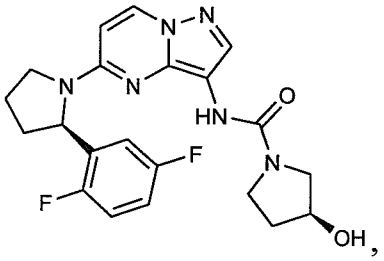
In some embodiments, the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof, is present in an amount from about 0.5 wt.% to about 7 wt.%. For example, the compound of formula **(I)**, a pharmaceutically acceptable salt thereof, or a combination thereof can be present in the liquid formulation in an amount of about 1.5 wt.% to about 2.5 wt.%.

In some embodiments, the compound of formula **(I)**, the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 5 mg/mL to about 50 mg/mL in the liquid formulation. For example, the compound of formula **(I)**, the pharmaceutically acceptable salt thereof, or the combination thereof, can have a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation. In some embodiments, the compound of formula **(I)**, the pharmaceutically acceptable salt thereof, or the combination

also includes a solubilizing agent and a base. The liquid formulation has a pH of about 2.5 to about 5.5. In some embodiments, the base includes a citrate (e.g., sodium citrate). The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

In one aspect, there is provided a liquid formulation comprising:

(S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof.

a solubilizing agent; and

a base;

wherein:

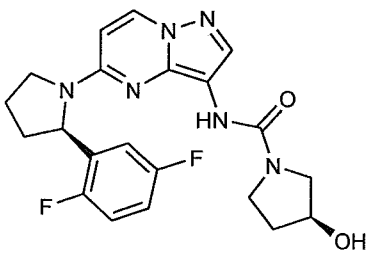
the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

In some embodiments, the liquid formulation has a pH of about 3 to about 4.

In some embodiments, the base includes sodium citrate dihydrate.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



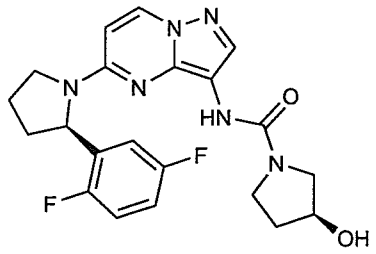
(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation includes a solubilizing agent, a buffer, a sweetener, a bitterness masking agent, and a flavoring agent. The liquid formulation has a pH of about 3 to about 4. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

In some embodiments, the buffer includes sodium citrate dihydrate.

In some embodiments, the sweetener includes sucrose.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



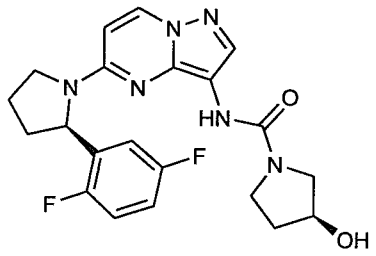
(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation

includes a solubilizing agent, a base, a sweetener, a bitterness masking agent, and a flavoring agent. The liquid formulation has a pH of about 3 to about 4. In some embodiments, the base includes a citrate (e.g., sodium citrate). The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

In one aspect, there is provided a liquid formulation comprising:

(S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof;

a solubilizing agent;

a base;

a sweetener;

a bitterness masking agent; and

a flavoring agent,

wherein:

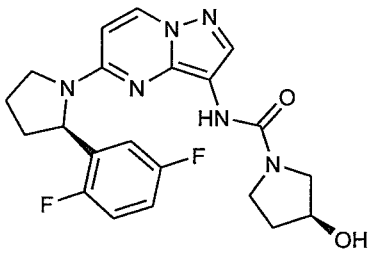
the formulation has a pH of about 3 to about 4; and

the compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 15 mg/mL to about 35 mg/mL in the liquid formulation.

In some embodiments, the base includes sodium citrate dihydrate.

In some embodiments, the sweetener includes sucrose.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:

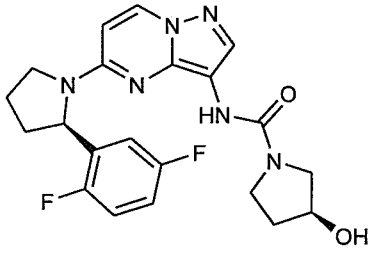


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation includes a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.% and a buffer present in an amount of about 0.1 wt.% to about 5 wt.%. The liquid formulation has a pH of about 2.5 to about 5.5. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

In one aspect, there is provided a liquid formulation comprising:

(S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof;

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

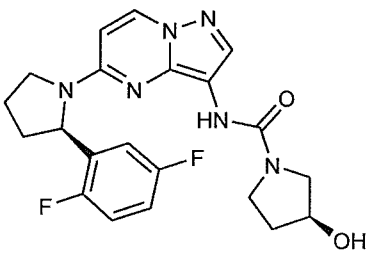
a base present in an amount of about 0.1 wt.% to about 5 wt.%;

wherein:

the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:

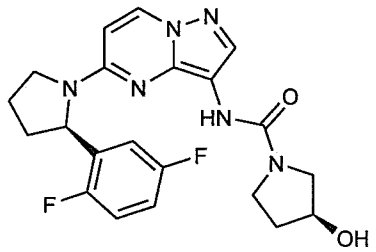


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation

includes a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%; a buffer present in an amount of about 0.1 wt.% to about 5 wt.%; a sweetener present in an amount of about 30 wt.% to about 70 wt.%; a bitterness masking agent present in an amount of about 0.2 wt.% to about 0.5 wt.%; and a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%. The liquid formulation has a pH of about 2.5 to about 5.5. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:

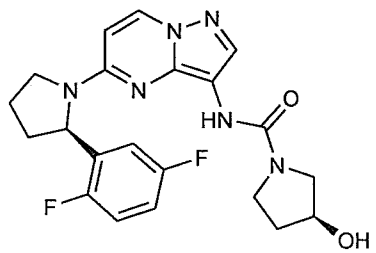


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation includes a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%; a base present in an amount of about 0.1 wt.% to about 5 wt.%; a sweetener present in an amount of about 30 wt.% to about 70 wt.%; a bitterness masking agent present in an amount of about 0.2 wt.% to about 0.5 wt.%; and a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%. The liquid formulation has a pH of about 2.5 to about 5.5. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

In one aspect, there is provided a liquid formulation comprising:

(S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof;

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

a base present in an amount of about 0.1 wt.% to about 5 wt.%;

a sweetener present in an amount of about 30 wt.% to about 70 wt.%;

a bitterness masking agent present in an amount of about 0.2 wt.% to about 0.5 wt.%; and

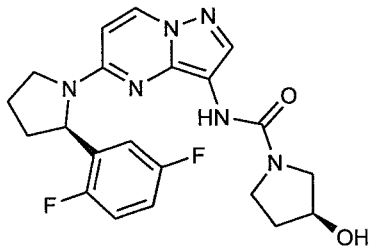
a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%,

wherein:

the formulation has a pH of about 2.5 to about 5.5; and

the compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

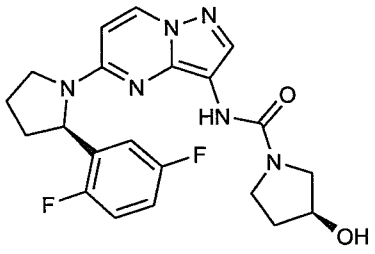
Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation includes a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%. The liquid formulation also includes a buffer including sodium citrate dihydrate present in an amount of about 0.1 wt.% to about 5 wt.%. The liquid formulation also includes a sweetener including sucrose present in an amount of about 30 wt.% to about 70 wt.%. The liquid formulation also includes a bitterness masking agent is present in an amount of about 0.2 wt.% to about 0.5 wt.%. The liquid formulation also includes a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%. The liquid formulation has a pH of about 3 to about 4. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:

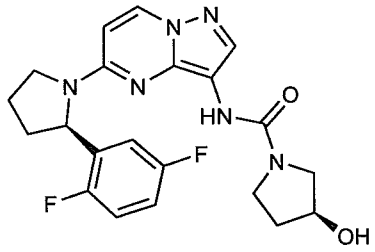


(I)

a pharmaceutically acceptable salt thereof, or a combination thereof. The liquid formulation includes a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%. The liquid formulation also includes a base including sodium citrate dihydrate present in an amount of about 0.1 wt.% to about 5 wt.%. The liquid formulation also includes a sweetener including sucrose present in an amount of about 30 wt.% to about 70 wt.%. The liquid formulation also includes a bitterness masking agent is present in an amount of about 0.2 wt.% to about 0.5 wt.%. The liquid formulation also includes a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%. The liquid formulation has a pH of about 3 to about 4. The compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

In one aspect, there is provided a liquid formulation comprising:

(S)-N-(5-((R)-2-(2,5-difluorophenyl)-pyrrolidin-1-yl)-pyrazolo[1,5-a]pyrimidin-3-yl)-3-hydroxypyrrolidine-1-carboxamide having the formula **(I)**:



(I)

a pharmaceutically acceptable salt thereof, or a combination thereof;

a solubilizing agent present in an amount of about 5 wt.% to about 35 wt.%;

a base comprising sodium citrate dihydrate present in an amount of about 0.1 wt.% to about 5 wt.%;

a sweetener comprising sucrose present in an amount of about 30 wt.% to about 70 wt.%;

a bitterness masking agent is present in an amount of about 0.2 wt.% to about 0.5 wt.%; and

a flavoring agent present in an amount of about 0.01 wt.% to about 2 wt.%,

wherein:

the formulation has a pH of about 3 to about 4; and

the compound of formula (I), the pharmaceutically acceptable salt thereof, or the combination thereof, has a concentration of about 20 mg/mL to about 30 mg/mL in the liquid formulation.

Also provided herein is a liquid formulation including (S)-N-(5-((R)-2-(2,5-

15.3±0.2, 16.5±0.2, 18.4±0.2, 19.2±0.2, 19.9±0.2, 20.2±0.2, 20.7±0.2, 21.5±0.2, 22.1±0.2, 23.1±0.2, 24.0±0.2. 24.4±0.2, 25.6±0.2, 26.5±0.2, 27.6±0.2, 28.2±0.2, 28.7±0.2, 30.8±0.2, and 38.5±0.2.

Also provided herein is a method of treating a cancer in a patient in need thereof. The method includes identifying a patient in need thereof having dysphagia and administering to the patient a therapeutically effective amount of a liquid formulation provided herein.

In one aspect, there is provided use of a therapeutically effective amount of the liquid formulation as described herein in the manufacture of a medicament for treating a cancer in a patient in need thereof, wherein the patient in need thereof has been identified as one having dysphagia.

Also provided herein is a method of treating a cancer in a patient in need thereof, which includes identifying a patient in need thereof having dysphagia, determining if the cancer is mediated by a Trk kinase and if the cancer is determined to be mediated by a Trk kinase, administering to the patient a therapeutically effective amount of a liquid formulation provided herein. In one aspect, there is provided use of a therapeutically effective amount of the liquid formulation as described herein in the manufacture of a medicament for treating a cancer in a patient in need thereof, wherein: the patient in need thereof has been identified as one having dysphagia; and the cancer has been determined to be mediated by a Trk kinase. Also provided herein is a method of treating a cancer in a patient in need thereof, which includes identifying a patient in need thereof having dysphagia, identifying that the cancer is mediated by a Trk kinase administering to the patient a therapeutically effective amount of a liquid formulation provided herein.

Also provided herein is a method of treating cancer in a patient in need thereof, which includes administering to the patient a therapeutically effective amount of a liquid formulation as provided herein. In one aspect, there is provided use of a therapeutically effective amount of the liquid formulation as described herein in the manufacture of a medicament for treating cancer in a patient in need thereof.

In some embodiments, the cancer is selected from the group consisting of a head and neck cancer, a throat cancer, an esophageal cancer, or combinations thereof.

In some embodiments, the patient is an infant, a child, an adolescent, or an elderly patient.

Also provided herein is a method for treating cancer in a subject in need thereof. The method includes determining if the cancer is associated with and/or exhibits one or more of overexpression, activation, amplification, and mutation of a Trk kinase and if the cancer is determined to be associated with and/or exhibits one or more of overexpression, activation, amplification, and mutation of a Trk kinase, administering to the subject a therapeutically effective amount of a liquid formulation as provided herein. In one aspect, there is provided use of a therapeutically effective amount of a liquid formulation as described herein in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the cancer is determined to be associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase. Also provided herein is a method for treating cancer in a subject in need thereof. The method includes identifying that the cancer is associated with and/or exhibits one or more of overexpression, activation, amplification, and mutation of a Trk kinase and administering to the subject a therapeutically effective amount of a liquid formulation as provided herein.

Also provided herein is a method for treating cancer in a subject in need thereof, which includes determining if the cancer is mediated by a Trk kinase, and if the cancer is determined to be mediated by a Trk kinase, administering to the subject a therapeutically

effective amount of a liquid formulation as provided herein. In one aspect, there is provided use of a therapeutically effective amount of a liquid formulation as described herein in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the cancer is determined to be mediated by a Trk kinase. Also provided herein is a method for treating cancer in a subject in need thereof, which includes identifying the cancer as mediated by a Trk kinase, and administering to the subject a therapeutically effective amount of a liquid formulation as provided herein.

Also provided herein is a method of treating a subject. The method includes performing an assay on a sample obtained from the subject to determine whether the subject has a dysregulation of a NTRK gene, a Trk protein, or expression or level of the same. The method also includes administering to a subject determined to have a dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same a therapeutically effective amount of a liquid formulation as provided herein. In one aspect, there is provided use of a therapeutically effective amount of a liquid formulation as described herein in the manufacture of a medicament for treating a subject, wherein the subject is determined to have dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same based on an assay that has been performed on a sample obtained from the subject to determine whether the subject has dysregulation of a NTRK gene, a Trk protein, or expression or level of the same.

In some embodiments, the dysregulation of a NTRK gene, a Trk protein, or expression or level of the same is a chromosome translation that results in the translation of a Trk fusion protein. The Trk fusion protein can be selected from the group consisting of: TP53-TrkA, LMNA-TrkA, CD74-TrkA, TFG-TrkA, TPM3-TrkA, NFASC-TrkA, BCAN-TrkA, MPRIP-TrkA, TPR-TrkA, RFWD2-TrkA, IRF2BP2-TrkA, SQSTM1-TrkA, SSBP2-TrkA, RABGAP1L-TrkA, C18ORF8-TrkA, RNF213-TrkA, TBC1D22A-TrkA, C20ORF112-TrkA, DNER-TrkA, ARHGEF2-TrkA, CHTOP-TrkA, PPL-TrkA, PLEKHA6-TrkA, PEAR1-TrkA, MRPL24-TrkA, MDM4-TrkA, LRRC71-TrkA, GRIPAP1-TrkA, EPS15-TrkA, DYNC2H1-TrkA, CEL-TrkA, EPHB2-TrkA, TGF-TrkA, NACC2-TrkB, QKI-TrkB, AFAP1-TrkB, PAN3-TrkB, SQSTM1-TrkB, TRIM24-TrkB, VCL-TrkB, AGBL4-TrkB, DAB2IP-TrkB, ETV6-TrkC, BTBD1-TrkC, LYN-TrkC, RBPMS-TrkC, EML4-TrkC, HOMER2-TrkC, TFG-TrkC, FAT1-TrkC, and TEL-TrkC.

In some embodiments, the dysregulation of a NTRK gene, a Trk protein, or expression or activity of the same is one or more point mutation in the gene. The NTRK gene can be a NTRK1 gene, and the one or more point mutations in the NTRK1 gene can result in the translation of a TrkA protein having substitutions are one or more of the following amino acid positions: 33, 336, 337, 324, 420, 444, 517, 538, 649, 682, 683, 702, and 1879.

In some embodiments, the one or more point mutations in the NTRK1 gene results in the translation of a TrkA protein having one or more of the following amino acid substitutions: R33W, A336E, A337T, R324Q, R324W, V420M, R444Q, R444W, G517R, G517V, K538A, R649W, R649L, R682S, V683G, R702C, and C1879T.

The features and advantages described in this summary and the following detailed description are not all-inclusive. Many additional features and advantages will be apparent to one of ordinary skill in the art in view of the drawings, specification, and claims hereof.

having XRPD diffraction peaks (2θ degrees) at 18.4±0.2, 20.7±0.2, 23.1±0.2, and 24.0±0.2.

56. The liquid formulation of claim 54, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 18.4±0.2, 20.7±0.2, 23.1±0.2, and 24.0±0.2.

57. The liquid formulation of claim 54, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 18.4±0.2, 19.2±0.2, 20.2±0.2, 20.7±0.2, 21.5±0.2, 23.1±0.2, and 24.0±0.2.

58. The liquid formulation of claim 54, wherein the crystalline form is characterized by having XRPD diffraction peaks (2θ degrees) at 10.7±0.2, 15.3±0.2, 16.5±0.2, 18.4±0.2, 19.2±0.2, 19.9±0.2, 20.2±0.2, 20.7±0.2, 21.5±0.2, 22.1±0.2, 23.1±0.2, 24.0±0.2. 24.4±0.2, 25.6±0.2, 26.5±0.2, 27.6±0.2, 28.2±0.2, 28.7±0.2, 30.8±0.2, and 38.5±0.2.

59. Use of a therapeutically effective amount of the liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating a cancer in a patient in need thereof, wherein the patient in need thereof has been identified as one having dysphagia.

60. Use of a therapeutically effective amount of the liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating a cancer in a patient in need thereof, wherein:

the patient in need thereof has been identified as one having dysphagia; and

the cancer has been determined to be mediated by a Trk kinase.

61. Use of a therapeutically effective amount of the liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating cancer in a patient in need thereof.

62. The use of claim 61, wherein the cancer is selected from the group consisting of a head and neck cancer, a throat cancer, an esophageal cancer, or combinations thereof.

63. The use of claim 61 or 62, wherein the patient is an infant, a child, an adolescent, or an elderly patient.

64. Use of a therapeutically effective amount of a liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the cancer is determined to be associated with one or more of overexpression, activation, amplification, and mutation of a Trk kinase.

65. Use of a therapeutically effective amount of a liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the cancer is determined to be mediated by a Trk kinase.

66. Use of a therapeutically effective amount of a liquid formulation according to any one of claims 1-58 in the manufacture of a medicament for treating a subject, wherein the subject is determined to have dysregulation of a NTRK gene, a Trk protein, or expression or activity, or level of the same based on an assay that has been performed on a sample obtained from the subject to determine whether the subject has dysregulation of a NTRK gene, a Trk protein, or expression or level of the same.

67. The use of claim 66, wherein the dysregulation of a NTRK gene, a Trk protein, or expression or level of the same is a chromosome translation that results in the translation of a Trk fusion protein.

68. The use of claim 67, wherein the Trk fusion protein is selected from the group consisting of: TP53-TrkA, LMNA-TrkA, CD74-TrkA, TFG-TrkA, TPM3-TrkA, NFASC-TrkA, BCAN-TrkA, MPRIP-TrkA, TPR-TrkA, RFWD2-TrkA, IRF2BP2-TrkA, SQSTM1-TrkA, SSBP2-TrkA, RABGAP1L-TrkA, C18ORF8-TrkA, RNF213-TrkA, TBC1D22A-TrkA, C20ORF112-TrkA, DNER-TrkA, ARHGEF2-TrkA, CHTOP-TrkA, PPL-TrkA, PLEKHA6-TrkA, PEAR1-TrkA, MRPL24-TrkA, MDM4-TrkA, LRRC71-TrkA, GRIPAP1-TrkA,

EPS15-TrkA, DYNC2H1-TrkA, CEL-TrkA, EPHB2-TrkA, TGF-TrkA, NACC2-TrkB, QKI-TrkB, AFAP1-TrkB, PAN3-TrkB, SQSTM1-TrkB, TRIM24-TrkB, VCL-TrkB, AGBL4-TrkB, DAB2IP-TrkB, ETV6-TrkC, BTBD1-TrkC, LYN-TrkC, RBPMS-TrkC, EML4-TrkC, HOMER2-TrkC, TFG-TrkC, FAT1-TrkC, and TEL-TrkC.

69. The use of claim 66, wherein the dyregulation of a NTRK gene, a Trk protein, or expression or activity of the same is one or more point mutation in the gene.

70. The use of claim 69, wherein the NTRK gene is a NTRK1 gene, and the one or more point mutations in the NTRK1 gene results in the translation of a TrkA protein having substitutions are one or more of the following amino acid positions: 33, 336, 337, 324, 420, 444, 517, 538, 649, 682, 683, 702, and 1879.

71. The use of claim 69, wherein the one or more point mutations in the NTRK1 gene results in the translation of a TrkA protein having one or more of the following amino acid substitutions: R33W, A336E, A337T, R324Q, R324W, V420M, R444Q, R444W, G517R, G517V, K538A, R649W, R649L, R682S, V683G, R702C, and C1879T.